The Influence of Vitamin a on Molecular Bio-mineral Tissue Development in Pigs (P02-012-19)

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Objectives: The objectives of this study were to identify differentially expressed transcripts and gene pathways in the vertebral bone of pigs receiving very high doses of vitamin A supplementation. Prior studies have ascertained that excessive vitamin A intake exhibits compartment-specific effects in bone tissue; these include regulating mineralisation genes in cortical bone containing bone marrow. Due to vertebral bone containing bone marrow, the hypothesis was that vitamin A will upregulate genes and pathways within vertebral bone that will favour bone mineralisation.

Methods: A total of 64 indoor UK pigs, fed standard commercial diets, were split into 8 groups ($n = 8$ per group) and received daily dosing of retinyl propionate (RP) (0 up to 10,000 µg RP/kg BW) for 17 weeks. Vertebral bone was sampled from the 13th thoracic vertebrae and RNA was extracted. RNA from control pigs and pigs receiving 10,000 µg RP/kg BW was labelled and hybridised on an Agilent 4*44k microarray. Genespring was used to identify differentially expressed transcripts, and Ingenuity Pathway Analysis (IPA) was applied to recognise gene pathways associated with vitamin A supplementation. qRT-PCR was then performed to confirm differential gene expression on selected biomarkers. Kruskal-Wallis test was used to determine significant changes in gene expression in response to vitamin A dose.

Results: A total of 318 transcripts were observed to be differentially regulated > 2-fold in the vertebral bone of pigs receiving 10,000 µg RP/kg BW, 199 transcripts (62.6%) were observed to be upregulated ($P < 0.05$). Genes relating to Rho-GTPases and regulation of cytoskeletal dynamics, such as *CDC42* and *FLNA*, persisted among canonical pathways ($P < 0.05$). qRT-PCR confirmed an 8.17-fold upregulation of *FLNA* in vertebral bone of pigs receiving 3000 µg RP/kg BW ($P < 0.01$), but no clear effect of treatment was observed on *CDC42* expression ($P = 0.147$).

Conclusions: Due to its role in the regulation of cytoskeletal reorganisation, of which subsequently affects both bone formation and resorption, the results suggest that high vitamin A intake potentially influences bone metabolism through interacting with the Rho-GTPase pathway.

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